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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,920	06/03/2002	Noriyuki Kizaki	025835-0104	8913

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EXAMINER	
PAK, YONG D	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,920	KIZAKI ET AL.	
	Examiner	Art Unit	
	Yong D Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-4,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-19,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/24/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/JP01/06619.

The amendment filed on June 17, 2004, amending claims 1-21 and adding claims 22-23, has been entered.

Claims 1-23 are pending.

Election/Restrictions

Applicant's election with traverse of Group II is acknowledged. The traversal is on the ground(s) that Groups II and III are linked to form a single inventive concept because there is at least one special technical feature common between the groups. Applicants also argue that prior to the amendment filed on June 1, 2004, clerical errors in the dependency of claims in Group II may have resulted in an improper restriction. This is not found persuasive because the technical feature linking the inventions of Group II-III does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art. Blattner et al. teach a DNA molecule that hybridises to SEQ ID NO:2 of the instant invention. The encoded polypeptide of Blattner et al. is a carbonyl reductase and one of skill in the art would recognize that said enzyme would reduce N-benzyl-3-pyrrolidinone to (S)-N-benzyl-3-pyrrolidinol. Accordingly, Groups II-III are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

The requirement is still deemed proper.

Claims 1-4 and 20-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

Notice of Possible Rejoinder: The Examiner notes that if claim 13 is found directed to an allowable product, then claims 20-21, which are directed to the process of making or using the patentable product, respectively, previously withdrawn from consideration as a result of a restriction requirement, would now be rejoined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86; see also MPEP 821.04, *In re Ochiai,* and *In re Brouwer*). Since process claims 20-21 would be rejoined and fully examined for patentability under 37 CFR 1.104, applicants are instructed to amend said claims as deemed necessary according to rejections made against the elected claims.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 24, 2002 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

Claim 5 is objected to as being dependent upon a non-elected base claim, and should be rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 5 has been interpreted to include all the limitations of its base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 7-19 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5 and 8-19 are drawn to a DNA molecule encoding a carbonyl reductase that reduces N-benzyl-3-pyrrolidinone to (S)-N-benzyl-3-pyrrolidinol using NADPH as a

coenzyme and having physical/chemical characteristics recited in claim 1 which do not provide any description on the structure of the polypeptide. Therefore, these claims are drawn to a genus of carbonyl reductase, with any structure and from any source. The specification only teaches one representative species, SEQ ID NO:2, from *Micrococcus luteus*. One representative species is not enough to describe the whole genus and there is no evidence on the record of the relationship between the structure of a *M. luteus* carbonyl reductase and the structure of a carbonyl reductase from another source. Therefore, the specification fails to describe other representative species of the genus of carbonyl reductase.

Claims 7 and 23 are drawn to DNA encoding a carbonyl reductase having 60% sequence identity to the DNA molecule of SEQ ID NO:2. Therefore, these claims are drawn to a genus of DNA having unlimited structure. A description of only 60% of the whole structure of SEQ ID NO:2 amounts to insufficient description of the structure of the DNA molecule in the claims. Therefore, these claims are drawn to a large variable genus of DNA molecules encoding polypeptides having an insufficient limitation on structure. The specification describes the DNA encoding a carbonyl reductase having SEQ ID NO:2. However, the specification fails to describe such a wide genus and therefore, many structurally unrelated polypeptides are encompassed within the scope of these claims.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention

in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 5, 7-19 and 23.

Claims 5 and 8-19 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that plasmids/microorganism(s) is/are required to practice the claimed invention. As a required element it/they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it/they is/are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the microorganism(s). See 37 C.F.R. § 1.802.

The specification does not provide a repeatable process for obtaining the microorganism(s) and it is not apparent if the microorganism(s) is/are readily available to the public. The specification must contain the date that the microorganism(s) was/were deposited, the name of the microorganism(s) and the address of where the microorganism(s) was/were deposited.

If the deposit(s) has/have been made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his/her signature, and registration number, stating that the specific strain(s)

has/have been deposited under the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

If the deposit(s) has/have not been made under the Budapest Treaty, then in order to certify that the deposit(s) meets the criteria set forth in 37 C.F.R. § 1.801-1.809, Applicant(s) may provide assurance of compliance by an affidavit or declaration, or by a statement by an Attorney of record over his/her signature and registration number, showing that:(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;(c) the deposit(s) will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;(d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807; and (e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 C.F.R. § 1.809 (d) should be added to the specification. See 37 C.F.R. § 1.803-1.809 for additional explanation of these requirements.

Claims 5, 7-19 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA molecule encoding the

carbonyl reductase of SEQ ID NO: 2, does not reasonably provide enablement for a DNA molecule encoding a polypeptide of unknown structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 5 and 8-19 are drawn to a DNA molecule encoding a carbonyl reductase having any structure and having the characteristics recited in claim 1. Claims 7 and 23 are drawn to a DNA molecule encoding a carbonyl reductase having at least 60% sequence identity to the DNA molecule of SEQ ID NO:2. Therefore, these claims are drawn to a genus of DNA having unlimited structure.

The structural limitations are as follows: only 60% of the whole structure of SEQ ID NO:2 or physical/chemical characteristics which do not elucidate the structure of the polypeptide. Therefore, these claims encompass polynucleotides encoding a carbonyl reductase having an unknown structure. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of constructs broadly encompassed by the claims. Also, despite knowledge in the art for the isolation of amino acids/polynucleotides, the specification fails to provide guidance regarding how to isolate other polynucleotides encoding a carbonyl reductase whose sequence is different from SEQ ID NO:2 or how to isolate polynucleotides encoding a carbonyl reductase from any organism having the characteristics recited in claim 1. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen a large number of possible combinations.

The predictability as to the level of conservation between the disclosed sequences and those of other carbonyl reductase is extremely complex. While recombinant techniques are available, it is not routine in the art to screen large numbers of amino acids where the expectation of obtaining similar sequences is unpredictable. The amino acid sequence determines the structural and functional properties of an enzyme. Knowledge of which sequences can be altered or removed and still result in similar protein activity is well outside the realm of routine experimentation.

Further, despite knowledge in the art for isolating polynucleotides, the specification fails to provide guidance regarding which amino acids of SEQ ID NO:1 are required to impart a polypeptide with the function of reducing N-benzyl-3-pyrrolidinone. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for modifications, as encompassed by the instant claims, and the positions within

a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity are limited in any protein and the result of such modifications is unpredictable.

The specification, which places weak limitation on the structure of the polypeptides as discussed above, does not support the broad scope of the claims because the specification does **not** establish: (A) regions of the carbonyl structure which may be modified without effecting reductase activity towards N-benzyl-3-pyrrolidinone; (B) the general tolerance of to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Therefore, one of ordinary skill would require guidance in order to make a DNA molecule encoding a polypeptide carbonyl reductase different from SEQ ID NO:2 in a manner reasonable correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-7 and 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 5 and 8-19, without the unit of measurement of the molecular weight, the molecular weight of "29,000" and "35,000" have no meaning.

In claims 6 and 22, the exact hybridization condition is unclear. Different nucleic acids hybridize to a DNA sequence under different conditions. Therefore, the scope of DNA molecules in claims 6 and 22 are unclear.

In claims 10-12, the claims are confusing because the DNA molecule of claim 5 only encodes the polypeptide of claim 1 and claims 10-12 requires that the DNA molecule of claim 5 encode the polypeptide of claim 1 and a glucose dehydrogenase.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-9, 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Blattner et al.

Blattner et al. teach a DNA molecule that hybridises to SEQ ID NO:2 of the instant invention. The encoded polypeptide of Blattner et al. is a carbonyl reductase and one of skill in the art would recognize that said enzyme would reduce N-benzyl-3-pyrrolidinone to (S)-N-benzyl-3-pyrrolidinol. Blattner et al. also teach a vector and transformant comprising said DNA molecule. Therefore, the teachings of Blattner et al. anticipate claims 8-9, 13 and 16.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner

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